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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/692,764	LEVY ET AL.	
	Examiner	Art Unit	
	Kimberly A. Makar, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,10,11,36-47,54 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,10,11,36-47,54 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 6/8/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's election without traverse of group II in the reply filed on 02/20/07 is acknowledged.

2. Claims 7, 9, 12-35, 48-53, and 55-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 02/20/07.

3. Applicant's election without traverse of a single disclosed tetracycline compound in the reply filed on 02/20/07 is acknowledged.

4. Applicant's cancellation of claims 7, 9, 12-35, 48-53, and 55-56 in the amendment dated 02/20/07 is acknowledged. Currently claims 1-6, 8,10-11, 36-47, 54, and 57 are pending.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1, 8, 11, 36-47 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims in EACH of U.S. Patent Nos. 6,500,812, 6,624,168, 6,642,270, 6,683,068, 6,818,634, 6,818,635, 6,833,365, 6,846,939, 6,849,615,7,045,507, and 7,094,806. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims represent a genus over claims in EACH of U.S. Patent Nos. 6,500,812, 6,624,168, 6,642,270, 6,683,068, 6,818,634, 6,818,635, 6,833,365, 6,846,939, 6,849,615, 7,045,507, 7,094,806 and 7,202,235.

7. The instant claims recite "A method for treating a subject for a DTMR, comprising: administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated." Thus, this method recites the single step of administering an effective amount of a tetracycline compound to a subject. The instant specification teaches no specific definition of DTMR (Disorders Treatable by Modulation of RNA), but recites a DTMR includes a "viral, neurodegenerative and other disorders which are caused or related to RNA function, structure, amounts and/or other activities of RNA which are lower or higher than desired and those disorders treatable by compounds described herein. Examples include viral disorders (e.g., retroviral disorders (e.g., HIV, etc.), disorders caused by human rhinovirus RNA and proteins,

VEE virus, Venezuelan equine encephalitis virus, eastern X disease, West Nile virus, bacterial spot of peach, camelpox virus, potato leafroll virus, stubborn disease and infectious variegations of citrus seedlings, viral protein synthesis in Escherichia coli infected with coliphage MS2, yellow viruses, citrus greening disease, ratoon stunting disease, European yellows of plants, inclusion conjunctivitis virus, meningopneumonitis virus, trachoma virus, hog plague virus, omithosis virus, influenza virus, rabies virus, viral abortion in ungulates, pneumonitis, and cancer (page 8-9 of the instant specification). Additional examples range from Alzheimer's disease, Huntington's Disease, ischemia, cystic fibrosis and a myriad of cancers (pages 9-10). Thus a DTMR reads on bacterial infections (citrus greening disease), viral infections (HIV), diseases, cancers, and fungal infections (pneumonitis).

8. U.S. Patent Nos. 6,500,812 (claims 14 and 15), 6,624,168 (claims 6-11), 6,642,270 (claims 6-14), 6,683,068 (claims 17-21), 6,818,634 (claims 27-29), 6,818,635 (claims 23-26), 6,833,365 (claims 20-26, and 33), 6,846,939 (claims 21-24), 6,849,615, (claims 6-10), 7,045,507 (claims 1-14, 22-55, 62-65, and 75) and 7,094,806 (claims 7-11) and 7,202,235 (claims 1-27, 34-46, and 49) recite methods of treating a subject with bacterial, fungal or tetracycline responsive states, an effective amount of tetracycline compounds and their derivatives. These methods teach the treatment of mammals, including humans. The instant claims 1, 8, 11, 36-47 recite methods of treating a DTMR with the single step of administering an effective amount of a tetracycline compound; the disclosed definition of a DTMR encompass the species diseases and disorders disclosed in the patents. Therefore, a method of treating a DTMR would include a

method of treating a bacterial infection, a fungal infection, or a tetracycline response using an effective amount of tetracyclines.

9. The claims in each patent are more narrowly drawn (representing the species) than the corresponding instant genus claims. Thus, the invention of the instant claims 1, 8, 11, 36-47 are not patentably distinct from those of respective patented claims.

Claims 1, 8, 11, 36-47 are directed to an invention not patentably distinct from claims of commonly assigned US patents 6,500,812, 6,624,168, 6,642,270, 6,683,068, 6,818,634, 6,818,635, 6,833,365, 6,846,939, 6,849,615, 7,045,507, 7,094,806 and 7,202,235. Specifically, the claims in each patent are more narrowly drawn (representing the species) than the corresponding instant genus claims.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 6,500,812, 6,624,168, 6,642,270, 6,683,068, 6,818,634, 6,818,635, 6,833,365, 6,846,939, 6,849,615, 7,045,507, 7,094,806 and 7,202,235, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

10. Claims 1, 8, 11, 36-47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application Nos. 10/692,563, 10/752,378, 10/786,881, 10943,571. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims represent a genus over claims in EACH of copending Application Nos. 10/692,563, 10/752,378, 10/786,881, 10/943,571.

11. The instant claims recite "A method for treating a subject for a DTMR, comprising: administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated." Thus, this method recites the single step of administering an effective amount of a tetracycline compound to a subject. A DTMR reads on bacterial infections (citrus greening disease), viral infections (HIV), diseases, cancers, and fungal infections (pneumonitis) (see above).

12. Copending Application Nos. 10/692,563, 10/752,378, 10/786,881, 10/943,571 recite methods of treating Malaria, a tetracycline responsive state, bacterial infections and killing a fungus comprising the administration of an effective amount of a tetracycline compound. The instant claims 1, 8, 11, 36-47 recite methods of treating a DTMR by administering an effective amount of a tetracycline compound; the disclosed

definition of a DTMR encompass the species diseases and disorders disclosed in the patent applications. Therefore, a method of treating a DTMR would include a method of treating a bacterial infection, a fungal infection, or a tetracycline response using an effective amount of tetracyclines.

13. The claims in each application are more narrowly drawn (representing the species) than the corresponding instant genus claims. Thus, the invention of the instant claims 1, 8, 11, 36-47 are not patentably distinct from those of respective application claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 8, 11, 36-47 are directed to an invention not patentably distinct from claims of commonly assigned US patent applications 10/692,563, 10/752,378, 10/786,881, 10/943,571. Specifically, the claims in each patent application are more narrowly drawn (representing the species) than the corresponding instant genus claims.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending applications 10/692,563, 10/752,378, 10/786,881, 10/943,571, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c),

either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-6, 8,10,11, 36-47, 54, and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims are drawn to a method of treating a disease treatable by Modulation of RNA (DMTR) comprising the administration of a tetracycline derivative compound to a subject in an effective amount. The method involves the modulation of subject's RNA from translation, message degradation,

translocation, binding capacity of RNA, and splicing of RNA. The method reads on treating humans.

16. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter., 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

17. *1) The nature of the invention.* The invention involves a method of treating *any* Disease Treatable by Modulation of RNA (DMTR) comprising the administration of *any* tetracycline derivative compound to *any* subject in an effective amount. The method involves the modulation of subject's RNA from translation, message degradation, translocation, binding capacity of RNA, and splicing of RNA, essentially any modulation of RNA in the subject. Furthermore, the method reads on treating humans.

18. *2) Number of working examples.* Applicants have provided multiple examples of making different tetracycline derivate compounds (see examples 1-2). Applicant's have provided a single example of the treatment of two independent murine macrophage cells lines (J774.2 and RAW 264.7) using in which there is up-regulation or down regulation of mRNA as assed by microarray technology (see example 3). There is no

disclosure if these murine macrophage cells are an art accepted model for a particular DMTR. Example 4 investigates the *in vitro* cytotoxicity of two tetracycline compound derivatives (minocycline and doxycycline) on Cos-1 and CHO-K1 cells and Example 5 investigates the *in vitro* anti-bacterial activity of 2 undisclosed tetracycline derivative compounds. There is no disclosure of an *in vivo* treatment of a particular DMTR in a working example. There is no disclosure in Example 3 of how the modulation of RNA occurs (translation, half-life, translocation, protein binding, or splicing) is effected by the exposure to the tetracycline derivatives. Applicant's do not disclose which particular genes are up-regulated or down regulated, but simply disclose the total up-regulated or down-regulated genes in table 3 (page 116 of the instant specification). There is no disclosure if the modulation of RNA results in any protein modulation.

19. *3) Amount of direction or guidance present.* The applicants provide very generic teaching of methods of treating a subject for a DTMR. The specification teaches that a DTMR includes a "viral, neurodegenerative and other disorders which are caused or related to RNA function, structure, amounts and/or other activities of RNA which are lower or higher than desired and those disorders treatable by compounds described herein. Examples include viral disorders (e.g., retroviral disorders (e.g., HIV, etc.), disorders caused by human rhinovirus RNA and proteins, VEE virus, Venezuelan equine encephalitis virus, eastern X disease, West Nile virus, bacterial spot of peach, camelpox virus, potato leafroll virus, stubborn disease and infectious variegations of citrus seedlings, viral protein synthesis in Escherichia coli infected with coliphage MS2, yellow viruses, citrus greening disease, ratoon stunting disease, European yellows of

plants, inclusion conjunctivitis virus, meningopneumonitis virus, trachoma virus, hog. plague virus, omithosis virus, influenza virus, rabies virus, viral abortion in ungulates, pneumonitis, and cancer (page 8-9 of the instant specification). Additional examples range from Alzheimer's disease, Huntington's Disease, ischemia, cystic fibrosis and a myriad of cancers (pages 9-10).

20. Applicant's single method step includes the "administering to said subject an effective amount of a tetracycline compound" but does not disclose how the single application of the tetracycline would differ from treating "bacterial spot of peach" to "HIV", other than to change the effective amount and the applications. Applicants do teach that the tetracycline compounds can be co-administered with a second agent "the second agent can be any agent which is known in the art to treat, prevent, or reduce the symptoms of a DTMR" including chemotherapeutic agents (page 93). Applicant further teach that the tetracycline compound can be administered as a pharmaceutical composition with a myriad of carriers, and methods of administration (page 94-9100). Applicants contend that the "effective amount" simply depends on size and weight of the subject, but then teaches that the choice of tetracycline compound can affect the "effective amount". Applicant's teaches, "[o]ne of ordinary skill in the art would be able to study the aforementioned factors and make the determination regarding the effective amount of the tetracycline compound without undue experimentation."

Applicant's further teach how actual dosages are determined by experimentation by the skilled artisan:

> Actual dosage levels of the active ingredients in the pharmaceutical compositions of this invention may be varied so as to obtain an amount of the active ingredient which is effective to achieve the desired therapeutic response for a particular patient,

composition, and mode of administration, without being toxic to the patient. The selected dosage level will depend upon a variety of factors including the activity of the particular compound of the present invention employed, or the ester, salt or amide thereof, the route of administration, the time of administration, the rate of excretion of the particular compound being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compound employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts.

A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the effective amount of the pharmaceutical composition required. For, example, the physician or veterinarian could start doses of the compounds of the invention employed in the pharmaceutical composition at levels lower than that required in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved.

In general, a suitable daily dose of a compound of the invention will be that amount of the compound which is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above. Generally, intravenous and subcutaneous doses of the compounds of this invention for a patient will range from about 0.0001 to about 100 mg per kilogram of body weight per day, more preferably from about 0.01 to about 50 mg per kg per day, and still more preferably from about 1.0 to about 100 mg per kg per day.

If desired, the effective daily dose of the active compound may be administered as two, three, four, five, six or more sub-doses administered separately at appropriate intervals throughout the day, optionally, in unit dosage forms. Page 100-101.

21. However, applicant does not teach how to evaluate which tetracycline compounds have what effect on different diseases? Or how they modulate RNA in different disease states? How would a skilled artisan decide between two different tetracycline derivatives?

22. Applicant's disclose hundreds of specific tetracycline compounds (pages 16-79), and teaches the disclosure of thousands of derivatives of those compounds, including all tautomers thereof (page 92). Do all tetracycline derivatives cause the exact same down-regulation or up-regulation of genes as those taught by applicant in example 3? Are they all modulated to the same extent? Would the modulation of RNA in murine macrophages be the same in human liver cells? Are there disease states where the

down-regulation of those genes disclosed by applicant in example 3 would actually exacerbate the disease state rather than "treat" and therefore actually be contraindicative to treat that particular DMTR?

23. Applicant fails to disclose the particular genes that are modulated in Example 3, table 3. What genes are these? Would the down regulation of these genes be detrimental in treating someone with Alzheimer's disease but beneficial for treating someone with cystic fibrosis? Applicant does not teach any specifics, other than to suggest that the skilled artisan would know how to decipher between the hundreds of compounds disclosed in the specification.

24. The invention as claimed reads on a method of treating any subject, including animals, and humans, using any tetracycline compound for any disease state. There is no teaching in the specification of how to alter the method of treating a naked mole rat suffering from Alzheimer's disease to treating a human suffering from prostate cancer.

25. *4) State of the art.* The art shows that chemically modified tetracyclines are highly variable. Liu et al (The lipophilicity, Pharmacokinetics, and Cellular Uptake of Different Chemically-Modified Tetracyclines (CMTs). Current medicinal Chemistry, 2001. 8:243-252) teaches that CMTs have great therapeutic potential not as antibiotics, but as therapeutic agents for disease states (see introduction, page 243), and that at least one CMT used in his study was currently being tested to treat humans (page 251, last paragraph). Liu studies 9 different CMTs (Figure 1). Liu teaches that different CMTs have different properties which effect cellular uptake, clearance, and half-life of the CMT. These differences can be seen between *in vivo* studies compared to *in vitro*

studies of the same CMT (page 243-244). Liu further teaches that the time for different CMTs to reach their peak maximum serum levels (C_{max}) and half-lives varied significantly Page 248-249, Figure 3 and Table 1). Liu suggest that these ranges may be the result of poor absorption from the gastrointestinal tract, in stability in the blood, rapid elimination from the serum (from urinary uptake, rapid detoxification or rapid tissue uptake), and that different organs showed different levels of uptake of the different CMTs (see page 249-250 and table 1). Liu further teaches that one CMT (CMT-7) tested was both unstable both in vitro and in vivo (page 250) and that the molecule was difficult to study because it is a tautomer and fluctuates between several forms (page 251). Liu stresses, "to asses the therapeutic potential of this series of compounds, their in vitro efficacy described above has to be "matched" to the pharmacokinetics, safety, and efficacy profile in vivo."

26. *5) Unpredictability of the art.* The art is highly unpredictable. The use of modified tetracycline compounds for uses other than antibiotics is growing, but the art reveals how these compounds react differently between in vitro and in vivo settings, as well as tissue-to tissue variability, and have high degrees of variability in serum levels and half-lifes. The art teaches that this variability is due to the structure of the tetracycline compound, but also to unknown *in vivo* environments which effect the tetracycline compound. Applicant's have not taught one of skill in the art how to decipher which of the thousands of tetracycline derivatives in the instant specification would be able to overcome known obstacles in the art. Applicant's have not shown any in vivo data to investigate the cellular uptake, half-life, clearance, etc. of the thousands of compounds

disclosed, not how to address these issues, other than altering the effective amount based on compound, and size and weight of the subject. A skilled artisan would therefore be required to determine how each of the thousands of tetracycline compounds react *in vivo* in order to determine which one to even begin testing for a particular DTMR. The skilled artisan would therefore be forced to conduct undue trial and error in order to practice the claimed invention, depending on which DMTR, which subject, and which tetracycline compound derivative was being utilized for treating the subject.

27. *6) Level of skill in the art.* The level of skill is high. The invention as claimed reads on a method of treating any subject, including animals, and humans. There is no teaching on how to adjust the method between different subjects. There is no teaching of how to decipher which tetracycline compounds are to be used for specific DMTRs, but not to be used for other DMTRs. Applicant's disclose thousands of tetracycline compounds, but only show 1 single example of RNA modulation in two murine macrophage cell lines after exposure to two tetracycline compounds. Applicant's do not disclose what genes are actually altered, nor if that alteration results in a modulation of proteins. Applicants teach that the only factors needed to determine "effective amount" is size and weight of the subject, and the choice of tetracycline compound, but does not teach how one of skill in the art would choose one derivative disclosed over another out of the thousands disclosed in the specification. Applicant' does not address known obstacles in the art regarding the administration of different tetracycline compounds. The skilled artisan would therefore be forces to conduct undue trial and error in order to

practice the claimed invention, depending on which DMTR, which subject, and which tetracycline compound derivative was being utilized for treating the subject.

28. *7) The breadth of the claims.* The breadth of the claims are broad. The invention as claim reads on a method of treating any subject, including animals, and humans, using any tetracycline compound for any disease state.

29. Given the above analysis of the factors which the courts have determined are critical in ascertaining whether a claimed invention is enabled, including the highly unpredictable art, the scarcity of working examples provided by applicant, the lack of guidance by the applicant, and the broad nature of the invention it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

30. Claims 1-6, 8,10,11, 36-47, 54, and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

31. Applicants claim a method of treating any subject for any Disorder treatable by Modulation of RNA (DMTR) comprising the administration to the subject an effective amount of any tetracycline compound. The method is further limited wherein the modulation of RNA is via translation, half-life, translocation, binding or splicing of the RNA and the subject is and animal. The method is further limited wherein the

tetracycline compound is a compound comprising thousands of a different tetracycline molecules comprising different side chains groups.

32. Thus the invention encompasses a treatment for any DMTR, on any subject sing any tetracycline compound. DMTRs are defined as "viral, neurodegenerative and other disorders which are caused or related to RNA function, structure, amounts and/or other activities of RNA which are lower or higher than desired and those disorders treatable by compounds described herein. Examples include viral disorders (e.g., retroviral disorders (e.g., HIV, etc.), disorders caused by human rhinovirus RNA and proteins, VEE virus, Venezuelan equine encephalitis virus, eastern X disease, West Nile virus, bacterial spot of peach, camelpox virus, potato leafroll virus, stubborn disease and infectious variegations of citrus seedlings, viral protein synthesis in Escherichia coli infected with coliphage MS2, yellow viruses, citrus greening disease, ratoon stunting disease, European yellows of plants, inclusion conjunctivitis virus, meningopneumonitis virus, trachoma virus, hog. plague virus, omithosis virus, influenza virus, rabies virus, viral abortion in ungulates, pneumonitis, and cancer" (page 8-9 of the instant specification). Additional examples range from Alzheimer's disease, Huntington's Disease, ischemia, cystic fibrosis and a myriad of cancers (pages 9-10). This definition is virtually open-ended, and reads on thousands of conditions and disease states.

33. The claims therefor read on a genus of methods of any in vivo or in vitro treatment of any DMTR in any subject using any tetracycline compound.

34. The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by

disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention.

35. In the instant case, applicants provide ample examples of making different tetracycline compounds (see examples 1-2), but do not, in fact, provide any data providing evidence for the in vivo treatment of any DMTR using any of these tetracycline compounds. Applicants do not provide explicit instructions on how to differentiate between the advantages of using one tetracycline compound over another, nor in what condition a particular tetracycline compound would be appropriate for, and which conditions that particular compound would be contraindicative for. Applicants instructions including altering the "effective amount" based on size and weight of the subject, and the compound used, but offer no details on how to determine what factors of size, weight, and more importantly, what compounds are to be considered for effective amount. The lone reference in vitro "treatment" of 2 murine macrophage cell lines, only demonstrates that there is an alteration of RNA as a result of the administration of 2 different tetracycline compounds. It does not disclose what DMTR that is supposed to be representative for, nor what genes are up-regulated or down-regulated. It does not disclose if those alterations resulted in protein modulation. Applicants do not disclose how, if the treatments utilized every tetracycline compound

within the scope of the claims, how one would overcome known obstacle in the art of modified tetracyclines (see above).

36. The skilled artisan would be unable to describe, or envision, any specific method for treating any specific DMTR in any subject using any tetracycline compound disclosed in the claims. The skilled artisan would therefore conclude that the applicants have not provided any examples of treating any specific DMTR in any subject using any tetracycline compound in vitro or in vivo in light of the instant specification and claims. The skilled artisan would conclude that applicant's were not in possession of the claimed invention.

37. It is noted that this Office Action contains rejections of the same claims under 35 USC 112, 1st (enablement and written description) and 35 USC 102 (b/e). While these rejections may seem contradictory, they are not because each is based upon a different legal analysis, i.e. sufficiency of the disclosure of the instant application to support claims under 35 USC 112, 1st paragraph vs. sufficiency of a prior art disclosure to anticipate or render obvious an embodiment(s) of the claimed invention (See *In re Hafner*, 161 USPQ 783 (CCPA 1969)).

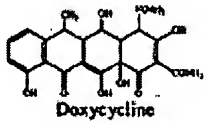
For purposes of prosecution, the following is defined:

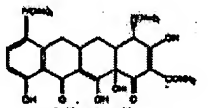
38. The specification teaches:

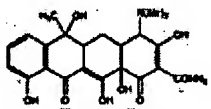
In an embodiment, when the DTMR is an aortic aneurysm, the tetracycline Compound is not doxycycline. In another embodiment, when the DTMR is Huntington's

disease, the tetracycline compound is not minocycline. In another embodiment, when the DTMR is cerebral ischemia, the tetracycline compound is not tetracycline. In other embodiments, when the DTMR is asthma, the tetracycline compound is not minocycline or doxycycline. Page 10.

The instant specification teaches the structures of substituted tetracycline compounds doxycycline, minocycline, as well as tetracycline:


Doxycycline


Minocycline


Tetracycline

Claim Rejections - 35 USC § 102

39. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

40. Claims 1, 2, 8, 10, 11, 36-38 are rejected under 35 U.S.C. 102(b) as being taught by Yrjanheikki et al (Tetracyclines Inhibit Microglial Activation and are Neuroprotective in Global Brain Ischemia. PNAS, 1998. 95:15769-15574). Claims 1,2,8,10,11 and 36-38 recite a method for treating a subject for a DTMR comprising administering an effective amount of a tetracycline compound, such that the DTMR is treated, wherein

said effective amount is effective to modulate translation of said subjects RNA, wherein the subject is an animal, and wherein the amount of at least one protein is modulated in the subject. The method is further limited wherein the tetracycline compound is a substituted compound comprising formula (I).

41. Yrjanheikki teaches the administration of the substituted tetracycline compounds doxycycline, minocycline, as well as tetracycline, prior to, and 30 minutes after, ischemia (see abstract, and Drug Treatment section page 15770). Yrjankeikki teaches that doxycycline and minocycline, but not tetracycline are neuroprotective, and minocycline inhibits induction of interleukin-1β-converting enzyme mRNA, decreases induction of iNOS mRNA, and prevents NOS protein expression (see page 15769, second column, 2nd full paragraph.) Yrjanheikki uses an *in vivo* model of a gerbil model of forebrain ischemia (see page15769-15770). Thus Yrjanheikki teaches the claimed invention.

42. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 6,500,812) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

43. Nelson et al (US Patent No. 6,500,812) teaches a method of treating a tetracycline response state in a mammal, comprising the administration of a tetracycline compound, such that the tetracycline state is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

44. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 6,624,168) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

45. Nelson et al (US Patent No. 6,624,168) teaches a method of treating a tetracycline response state in a mammal, comprising the administration of a tetracycline compound, such that the tetracycline state is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome

either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

46. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 6,642,270) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

47. Nelson et al (US Patent No. 6,642,270) teaches a method of treating a tetracycline response state in a mammal, comprising the administration of a tetracycline compound, such that the tetracycline state is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

48. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 6,683,068) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to

said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

49. Nelson et al (US Patent No. 6,683,068) teaches a method of treating a bacterial infection in a human, comprising the administration of a tetracycline compound, such that the bacterial infection is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

50. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 6,818,634) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

51. Nelson et al (US Patent No. 6,818,634) teaches a method of treating a tetracycline response state in a mammal, comprising the administration of a tetracycline compound, such that the tetracycline state is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

52. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 6,818,635) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

53. Nelson et al (US Patent No. 6,818,635) teaches a method of treating a *Cryptosporidium parvum* disorder in a human, comprising the administration of a tetracycline compound, such that the *Cryptosporidium parvum* disorder is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

54. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 6,846,939) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

55. Nelson et al (US Patent No. 6,846,939) teaches a method of treating a bacterial infection in a subject, comprising the administration of a tetracycline compound, such that the bacterial infection is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

56. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 6,849,615) listed in applicant's IDS form dated 06/08/06.

Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

57. Nelson et al (US Patent No. 6,849,615) teaches a method of treating a tetracycline response state in a mammal, comprising the administration of a tetracycline compound, such that the tetracycline state is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

58. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Draper et al (US Patent No. 7,045,507) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

59. Draper et al (US Patent No. 7,045,507) teaches a method of treating a fungal infection, comprising the administration of a tetracycline compound, such that the fungal infection is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

60. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 7,094,806) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

61. Nelson et al (US Patent No. 7,094,806) teaches a method of treating a tetracycline response state in a mammal, comprising the administration of a tetracycline compound, such that the tetracycline state is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome

either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

62. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent No. 7,202,235) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

63. Nelson et al (US Patent No. 7,202,235) teaches a method of treating a *Cryptosporidium parvum* disorder in a human, comprising the administration of a tetracycline compound, such that the *Cryptosporidium parvum* disorder is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

64. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Draper et al (US Patent Publication No. US 20040242548) listed in applicant's IDS

form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

65. Draper et al (US Patent Publication No. US 20040242548) teaches a method of treating malaria in a subject, comprising the administration of a tetracycline compound, such that malaria is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

66. Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Huss et al (US Patent Publication No. US 20040266740) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

67. Huss et al (US Patent Publication No. US 20040266740) teaches a method of treating a tetracycline responsive state in a human, comprising the administration of a tetracycline compound, such that the tetracycline state is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al (US Patent Publication No. US 20050026876) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

68. Nelson et al (US Patent Publication No. US 20050026876) teaches a method of treating a tetracycline responsive state in a mammal, comprising the administration of a tetracycline compound, such that the tetracycline state is treated (see abstract and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1, 8, 11, 36-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Draper et al (US Patent Publication No. US 20050070510) listed in applicant's IDS form dated 06/08/06. Claims 1,8,11,36-47 recite a method of treating a DTMR comprising administering to said subject an effective amount of a tetracycline compound, such that said DTMR is treated, wherein the subject is an animal, and using a variety of substituted tetracycline compounds. This method reads on treating bacterial, fungal, and general disease states (see specification page 8-10).

69. Draper et al (US Patent Publication No. US 20050070510) teaches a method of treating a fungus and fungal infection, comprising the administration of a tetracycline compound, such that the fungal infection is treated (see abstract, body and claims).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Conclusion

70. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kam/04/25/07

DAVID GUZO
PRIMARY EXAMINER